

Claims

1. A transcriptional regulator comprised of RNA.
2. A transcriptional regulator comprising:
5 a DNA-binding moiety; and
an RNA linked to the DNA binding moiety, the RNA having transcriptional regulatory activity.
3. The transcriptional regulator of claim 2 wherein the DNA-binding moiety is selected from the group consisting of nucleic acids, polypeptides, intercalation compounds, and chemicals that demonstrate specific DNA binding.
4. The transcriptional regulator of claim 2 wherein the regulatory RNA is characterized by an ability, when recruited to a DNA site operationally linked to a promoter, to activate
15 transcription from that promoter at least two-fold.
5. The transcriptional regulator of claim 2 wherein the regulatory RNA is characterized by an ability, when recruited to a DNA site operationally linked to a promoter, to activate transcription from that promoter to a level at least half that observed when the promoter is
20 activated by Gal4 bound to a similarly-positioned site.
6. The transcriptional regulator of any one of claims 2, 4, or 5, wherein the regulatory RNA has a structure comprising a stem-loop.

7. The transcriptional regulator of claim 6 wherein the stem includes at least about 6 base pairs.

8. The transcriptional regulator of claim 6 wherein the stem includes at least about 10 basepairs.

9. The transcriptional regulatory of claim 7 wherein the regulatory RNA has a sequence comprising 5'-UGC(G>U>A)GG(U>A>C)(U>ACG)(C>A)(G>A>U)-3' (SEQ ID NO:4).

10. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator, when recruited to a site operationally linked to a promoter, increases transcription from that promoter.

11. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator, when recruited to a site operationally linked to a promoter, decreases transcription from that promoter.

12. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator affects transcription initiation.

13. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator affects elongation.

14. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator affects a process selected from the group consisting of reinitiation, termination, and pausing.

5 15. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator is active in one or more cell type selected from the group consisting of bacterial cells, yeast cells, mammalian cells, insect cells, plant cells, reptile cells, celenorate cells, and protozoan cells.

10 16. The transcriptional regulator of claim 15 wherein the regulator is active in yeast, mouse, or human cells.

17. The transcriptional regulator of claim 16 wherein the regulator is active in yeast and human cells.

15 18. The transcriptional regulator of claim 1 or claim 2 wherein the regulator is active at more than one gene in a given cell.

19. The transcriptional regulator of claim 10 wherein the regulator's activity is squelched in yeast cells by over-expression of Gal4.

20 20. The transcriptional regulator of claim 10 wherein the regulator functions as an acidic activator.

21. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator is constitutively active.

22. The transcriptional regulator of claim 1 or claim 2, which transcriptional regulator is conditionally active.

23. An RNA transcriptional regulator identified by a method comprising steps of:
providing a library of RNA molecules linked to an RNA comprising recruiting moiety;
expressing the linked library of RNA molecules in a cell that also expresses an interacting moiety linked to a DNA binding moiety that specifically recognizes a site operatively linked to a promoter directing expression of a detectable gene, which interacting moiety associates with the recruiting moiety;
detecting an increase or decrease in expression of the detectable gene; and
designating those RNA molecules present in cells in which expression of the detectable gene is increased or decreased as riboregulators.

24. A method of identifying RNA transcriptional regulators, the method comprising steps of:
providing a population of RNA molecules;
delivering the RNA molecules to a location operationally linked to a promoter; and
identifying those RNA molecules within the population that alter the rate or amount of transcription from the promoter.

25. The method of claim 24 wherein the step of identifying comprises identifying those RNA molecules that effect at least a two-fold change in the rate or extent of transcription from the promoter.

5 26. The method of claim 24 wherein the step of identifying comprises identifying those RNA molecules that effect at least a five-fold change in the rate or extent of transcription from the promoter.

10 27. The method of claim 24 wherein the step of identifying comprises identifying those RNA molecules that effect at least a ten-fold change in the rate or extent of transcription from the promoter.

15 28. The method of claim 24 where in the step of identifying comprises identifying those RNA molecules that effect at least a one hundred-fold change in the rate or extent of transcription from the promoter.

20 29. The method of claim 24 where in the step of identifying comprises identifying those RNA molecules that effect at least a one thousand-fold change in the rate or extent of transcription from the promoter.

30. A therapeutic composition comprising:
an RNA molecule characterized by an ability to alter transcription from a promoter when recruited to a site operatively linked to that promoter; and
a pharmaceutically acceptable carrier.

31. A method of treating an individual suffering from a disorder whose symptoms are alleviated or cured by effecting a change in expression of a gene, the method comprising steps of:

identifying an individual suffering from a disorder whose symptoms are alleviated or cured by effecting a change in expression of a gene; and

administering to the individual an RNA molecule characterized in that, when the RNA molecule is recruited to a site operationally linked to the gene promoter, it effects the change in expression of the gene.

32. A method of identifying a target RNA that interacts with a test RNA, the method comprising steps of:

providing a first hybrid RNA molecule comprising a riboregulator linked to a test RNA;

providing a library of second hybrid RNA molecules, each of which comprises a potential target RNA linked to an interacting RNA;

providing a third hybrid polypeptide molecule comprising an interacting polypeptide, which interacting polypeptide associates with the interacting RNA, linked to a DNA binding moiety, which DNA binding moiety binds to a site operationally linked to a promoter directing expression of a detectable gene;

expressing the first, second, and third hybrids in a cell also containing the gene under control of the promoter and operationally linked to the site;

detecting those cells in which expression of the gene is altered; and

classifying the potential target RNA of the library member in the detected cell as an RNA that interacts with the test RNA.

33. A method of identifying a target RNA that interacts with a test RNA, the method comprising steps of:

providing a library of first hybrid RNA molecules, each of which comprises a riboregulator linked to a potential target RNA;

5 providing a second hybrid RNA molecule, comprising a test RNA linked to an interacting RNA;

providing a third hybrid polypeptide molecule comprising an interacting polypeptide, which interacting polypeptide associates with the interacting RNA, linked to a DNA binding moiety, which DNA binding moiety binds to a site operationally linked to a promoter directing expression of a detectable gene;

expressing the first, second, and third hybrids in a cell also containing the gene under control of the promoter and operationally linked to the site;

detecting those cells in which expression of the gene is altered; and

15 classifying the potential target RNA of the library member in the detected cell as an RNA that interacts with the test RNA.

34. A method of identifying a target protein that interacts with a test RNA, the method comprising steps of:

20 providing a first hybrid RNA molecules, comprising a riboregulator linked to a test RNA;

providing a library of second hybrid polypeptide molecules, each of which comprises a potential target polypeptide linked to a DNA binding polypeptide, which DNA binding polypeptide binds to a site operationally linked to a promoter directing expression of a detectable gene;

expressing the first and second third hybrids in a cell also containing the gene under control of the promoter and operationally linked to the site;

detecting those cells in which expression of the gene is altered; and

classifying the potential target polypeptide of the library member in the detected cell as a target polypeptide that interacts with the test RNA.

35. A method of identifying a target RNA that interacts with a test polypeptide, the method comprising steps of:

providing a library of first hybrid RNA molecules, each of which comprises a riboregulator linked to a potential target RNA;

providing a second hybrid polypeptide molecule comprising a test polypeptide linked to a DNA binding moiety, which DNA binding moiety binds to a site operationally linked to a promoter directing expression of a detectable gene;

expressing the first and second hybrids in a cell also containing the gene under control of the promoter and operationally linked to the site;

detecting those cells in which expression of the gene is altered; and

classifying the potential target RNA of the library member in the detected cell as a target RNA that interacts with the test polypeptide.

36. An RNA linker molecule comprising a first portion that interacts with a first interaction partner and a second portion that interacts with a second interaction partner.